

REMARKS/ARGUMENTS

Claims 1 to 60 are pending in this application. Restriction has been required under 35 U.S.C. § 121 between:

Group	Claims	Subject Matter	Class
1	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is CR ³ X is (CR ⁹ R ¹⁰) _m	585/1+
2	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is CR ³ X is NR ¹¹	564/1+
3	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is CR ³ X is O(CR ⁹ R ¹⁰) _m	568/ 256+
4	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is N X is (CR ⁹ R ¹⁰) _m	564/ 200+
5	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is N X is NR ¹¹	564/ 1.5+
6	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is N X is O(CR ⁹ R ¹⁰) _m	568/3+
7	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P X is (CR ⁹ R ¹⁰) _m	568/8+
8	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P X is NR ¹¹	510/ 467+
9	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P X is O(CR ⁹ R ¹⁰) _m	568/ 10+
10	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P=O X is (CR ⁹ R ¹⁰) _m	562/4+
11	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P=O X is NR ¹¹	562/4+
12	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P=O	562/4+

Group	Claims	Subject Matter	Class
		X is $O(CR^9R^{10})_m$	
13	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P=S X is $(CR^9R^{10})_m$	568/8+
14	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P=S X is NR^{11}	568/8+
15	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is P=S X is $O(CR^9R^{10})_m$	562/8+
16	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is As X is $(CR^9R^{10})_m$	556/ 30+
17	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is As X is NR^{11}	556/ 30+
18	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is As X is $O(CR^9R^{10})_m$	562/ 30+
19	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is As=O X is $O(CR^9R^{10})_m$	562/ 45+
20	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is As=O X is NR^{11}	562/ 45+
21 (same as 19)	1 to 7 in part, 26, 43, 45 to 46	Compounds and compositions where A is As=O X is $O(CR^9R^{10})_m$	562/ 45+
22	1 to 7 in part, 26, 43	Compounds and compositions where A is $-[C(L)R^{12}(CR^{13}R^{14})_a]_b-$ X is $O(CR^9R^{10})_m$	585/1+
23	1 to 7 in part, 26, 43	Compounds and compositions where A is $-[C(L)R^{12}(CR^{13}R^{14})_a]_b-$ X is NR^{11}	585/1+
24 (same as 22)	1 to 7 in part, 26, 43	Compounds and compositions where A is $-[C(L)R^{12}(CR^{13}R^{14})_a]_b-$ X is $O(CR^9R^{10})_m$	581/1+
25	1 to 7 in part, 26, 43	Compounds and compositions where A is $-[N(L)C(W)(CR^{15}R^{16})_c]_d-$ X is $O(CR^9R^{10})_m$	534/1+
26	1 to 7 in part,	Compounds and compositions where	534/1+

Group	Claims	Subject Matter	Class
(same as 25)	26, 43	A is $-\text{[N(L)C(W)(CR}^{15}\text{R}^{16})_c]_d-$ X is $\text{O(CR}^9\text{R}^{10})_m$	
27	1 to 7 in part, 26, 43	Compounds and compositions where A is $-\text{[N(L)C(W)(CR}^{15}\text{R}^{16})_c]_d-$ X is NR^{11}	534/1+
28	1 to 7 in part, 26, 43	Compounds and compositions where A is $-\{[\text{NR}^{20}\text{C(W)C(L)R}^{21}(\text{CR}^{22}\text{R}^{23})_g]_h$ $(\text{NR}^{24}\text{C(W)(CR}^{25}\text{R}^{16})_{ij})-(\text{L)R}^{12}(\text{Cr}^{13}\text{R}^{14})_a]_b-$ X is $(\text{CR}^9\text{R}^{10})_m$	534/1+
29	1 to 7 in part, 26, 43	Compounds and compositions where A is $-\{[\text{NR}^{20}\text{C(W)C(L)R}^{21}(\text{CR}^{22}\text{R}^{23})_g]_h$ $(\text{NR}^{24}\text{C(W)(C R}^{25}\text{R}^{16})_{ij})-(\text{L)R}^{12}(\text{Cr}^{13}\text{R}^{14})_a]_b-$ X is $\text{O(CR}^9\text{R}^{10})_m$	534/1+
30	1 to 7 in part, 26, 43	Compounds and compositions where A is $-\{[\text{NR}^{20}\text{C(W)C(L)R}^{21}(\text{CR}^{22}\text{R}^{23})_g]_h$ $(\text{NR}^{24}\text{C(W)(C R}^{25}\text{R}^{16})_{ij})-(\text{L)R}^{12}(\text{Cr}^{13}\text{R}^{14})_a]_b-$ X is NR^{11}	534/1+
31 (same as 30)	1 to 7 in part, 26, 43	Compounds and compositions where A is $-\{[\text{NR}^{20}\text{C(W)C(L)R}^{21}(\text{CR}^{22}\text{R}^{23})_g]_h$ $(\text{NR}^{24}\text{C(W)(C R}^{25}\text{R}^{16})_{ij})-(\text{L)R}^{12}(\text{Cr}^{13}\text{R}^{14})_a]_b-$ X is NR^{11}	534/1+
32	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is CR^3 X is $(\text{CR}^9\text{R}^{10})_m$	424/ 1.37+
33	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is CR^3 X is NR^{11}	424/ 1+ or 534/ 10+
34	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is CR^3 X is $\text{O(CR}^9\text{R}^{10})_m$	424/ 1.38+ or 534/ 10+
-- (no #)	8 to 13, 32, 47 to 48, 53, 59 to	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where	424/ 1.37+

Group	Claims	Subject Matter	Class
	60 in part	A is N X is $(\text{CR}^9\text{R}^{10})_m$	or 534/ 10+
35	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is N X is NR^{11}	424/ 1.37+ or 534/ 10+
36	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is N X is $\text{O}(\text{CR}^9\text{R}^{10})_m$	424/ 1.38+ or 534/ 10+
37 (same as 34)	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is CR^3 X is $\text{O}(\text{CR}^9\text{R}^{10})_m$	424/ 1.38+ or 534/ 10+
38	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is $\text{P}=\text{O}$ X is $(\text{CR}^9\text{R}^{10})_m$	424/ 1.37+ or 534/ 10+
39	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is $\text{P}=\text{O}$ X is NR^{11}	424/ 1.37+ or 534/ 10+
40	8 to 13, 32, 47 to 48, 53, 59 to 60 in part	Radiopharmaceutical compounds containing a radionuclide and a tripodal compound where A is $\text{P}=\text{O}$ X is $\text{O}(\text{CR}^9\text{R}^{10})_m$	424/ 1.38+ or 534/ 10+
41	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is CR^3 X is $(\text{CR}^9\text{R}^{10})_m$	424/ 9.3+
42	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is CR^3 X is NR^{11}	424/ 9.3+

Group	Claims	Subject Matter	Class
43	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is CR^3 X is $\text{O}(\text{CR}^9\text{R}^{10})_m$	424/ 9.3+
44	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is N X is $(\text{CR}^9\text{R}^{10})_m$	424/ 9.3+
45	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is N X is NR^{11}	424/ 9.3+
46	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is N X is $\text{O}(\text{CR}^9\text{R}^{10})_m$	424/ 9.3+
47 (same as 43)	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is CR^3 X is $\text{O}(\text{CR}^9\text{R}^{10})_m$	424/ 9.3+
48	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is $\text{P}=\text{O}$ X is $(\text{CR}^9\text{R}^{10})_m$	424/ 9.3+
49	14 to 19 in part, 40, 51 to 52	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is $\text{P}=\text{O}$ X is NR^{11}	424/ 9.3+
50	20 to 25 in part, 36, 49 to 50	MRI compounds containing a paramagnetic metal ion and a tripodal compound where A is $\text{P}=\text{O}$ X is $\text{O}(\text{CR}^9\text{R}^{10})_m$	424/ 9.3+
51	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is CR^3 X is $(\text{CR}^9\text{R}^{10})_m$	424/ 9.4+
52	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is CR^3	424/ 9.4+

Group	Claims	Subject Matter	Class
		X is NR ¹¹	
53	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is CR ³ X is O(CR ⁹ R ¹⁰) _m	424/ 9.4+
54	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is N X is (CR ⁹ R ¹⁰) _m	424/ 9.4+
55	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is N X is NR ¹¹	424/ 9.4+
56	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is N X is O(CR ⁹ R ¹⁰) _m	424/ 9.4+
57 (same as 53)	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is CR ³ X is O(CR ⁹ R ¹⁰) _m	424/ 9.4+
58	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is P=O X is (CR ⁹ R ¹⁰) _m	424/ 9.4+
59	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is P=O X is NR ¹¹	424/ 9.4+
60	20 to 25 in part, 36, 49 to 50	X-ray or CT contrast agents containing a heavy metal ion of atomic number 21 to 31, 39 to 50, 56 to 80, 82, 83, 90 and tripodal compounds where A is P=O X is O(CR ⁹ R ¹⁰) _m	424/ 9.4+

Group	Claims	Subject Matter	Class
61	27 to 31 in part	Methods for treating bone disorders	424/ 1.11+
62	33 to 35 in part	Methods of radioactive imaging	424/ 9.3+
63	37 to 39	Methods of MRI imaging	424/ 9.35+
64	44	Methods of performing X-ray	424/ 9.4+
65	54 to 58 in part	Compositions and methods of use thereof	424/ 1.11+

It is asserted that the inventions of Groups 1 to 65 are related as product (Groups 1 to 60) and process of use (Groups 61 to 65). A requirement has also been made for an election of species. It is alleged that claims 1 to 60 are directed to improper Markush-type generic claims requiring restriction under 35 U.S.C. § 121, allegedly because the groups do not contain "an immutable central core structure" and they do not contain a "fundamental common core structure" that can be attributed to a biological activity." Applicant traverses the restriction requirement, in general and, more specifically, the allegation that the claims contain improper Markush groups for examination.

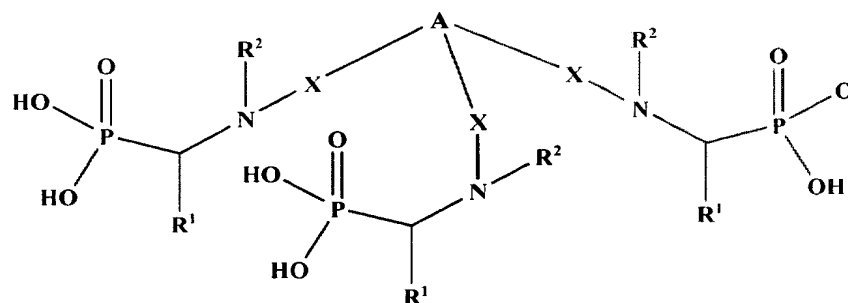
According to MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

- (A) The inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05 to § 806.05(i)); and
- (B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a) to § 806.04(i), § 808.01(a), and § 808.02).

For purposes of the initial requirement, a serious burden may be *prima facie* shown if the examiner shows separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. In the subject application, the claims have been **restricted into 65 different groups**, however, these groups have only been **classified into nine different classes**, namely Class 424, Class 510, Class 534, Class 556, Class 562, Class 564,

Class 568, Class 581 and Class 585. As the restriction requirement is currently drawn, *applicant would be required to file more than 60 divisional applications to cover the subject matter of the original application.* It is respectfully submitted that this is unduly burdensome to the applicant. At a minimum, applicant respectfully requests reconsideration with respect to a reduction in the number of groups from 65 to nine.

It is alleged that claims 1 to 60 are directed to improper Markush-type generic claims requiring restriction under 35 U.S.C. § 121, allegedly because the groups do not contain “an immutable central core structure” and they do not contain a “‘fundamental common core structure’ that can be attributed to a biological activity.” Applicant wishes to point out that there is an immutable central core structure attributed to the activity of the compound, namely three aminophosphonate chelating arms, each of which contains three donor atoms (see page 10, lines 23 to 28). The office action implies that none of the claimed chelants have anything in common structurally or functionally. This is simply not the case. All of the chelants have the following core structure:



And while there is variability at certain locations within the chelant (for example, at A and X), all of the chelants contain three aminophosphonate groups (the red, blue and green arms labelled above). However, applicant believes that it is in no way improper to present claims that delineate the full scope of his invention. Applicant is unaware of any requirement under

the law requiring him to limit his claims to a single species or, at least, to a subgenus of a single classification.

While applicant does not believe that a proper requirement for restriction has been established, applicant believes that any restriction among the members of the Markush groups within the claims should only be made *provisionally*. MPEP § 803.02, which addresses restriction practice with respect to Markush-type claims, clearly sets forth that the Examiner may only require a *provisional* election of a single species prior to examination on the merits. The provisional election would be given effect in the event that the Markush-type claim was found not to be allowable. Following election, the Markush-type claim would be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim were not allowable over the prior art, examination would be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration. However, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim would then be extended.

The MPEP provides an example in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E. With such a claim, the examiner may require a *provisional* election of a single species (CA, CB, CC, CD, or CE). The Markush-type claim is then examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If, on examination, the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species would be rejected, and claims to the non-elected species would be held withdrawn from further consideration. On the other hand, if no prior art anticipates or renders obvious the elected species, the search of the Markush-type claim would then be extended.

DOCKET NO.: PH-7124 US (BMS-2293)

PATENT

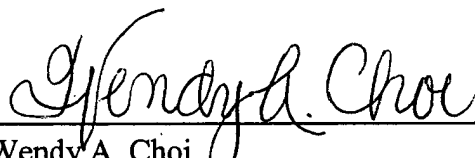
Application No.: 10/033,770

Office Action Dated: June 5, 2003

Thus, applicant respectfully requests reconsideration of the requirement for restriction, and in particular an indication that the requirement is only a provisional election for the purpose of carrying out the search. Nonetheless, to be fully responsive to the restriction requirement, applicant elects *with traverse* to prosecute the claims of **Group 4** [tripodal chelant where A is N and X is (CR₉R₁₀)_m]. Further, applicant elects *with traverse* the compound **tris(2-aminoethyl)amine-N,N',N''-tris(2-hydroxybenzyl)methylene phosphonic acid [Tren(HBP)₃]** exemplified in Example 1.

If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (215) 557-3861. A petition for a one-month extension of time is filed herewith.

Date: July 10, 2003


Wendy A. Choi
Registration No. 36,697

WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439